Can Prolaris Score be used to predict change in Gleason Score from biopsy to post-radical prostatectomy pathology?

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Can Prolaris Score be used to predict change in Gleason Score from biopsy to post-radical prostatectomy pathology?

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Background

- Early detection of prostate cancer (PCa) and the increasing popularity of active surveillance necessitate the development and refinement of risk stratification tools.
- While Gleason Score (GS) serves a valuable prognostic role, a relatively high rate of discordance[1] between biopsy and post-surgical pathology necessitates either additional prognostic tests or a method to predict the likelihood of grade discrepancy.
- Genomic analysis has emerged as a reliable method to improve risk stratification for men with prostate cancer, especially for those with low- and intermediate-risk disease, in whom conservative management is an option.
- The Cell Cycle Progression Score (CCPS) – or Prolaris Score (Myriad Genetics) – measures expression of genes involved in Cell Cycle Progression. It has been validated in numerous settings as a predictor of cancer-related death and biochemical recurrence.[2,3] The score is used to predict whether an individual's cancer is more aggressive, less aggressive, or consistent with others in his AUA risk group.
- Thus far, the ability of the CCPS to predict a change in GS between biopsy and post-surgical pathology has not been evaluated.

Problem Statement

In the context of a significant rate of discrepancy in prostate cancer pathologic grading between biopsy and post-surgical analysis, this project seeks to determine whether or not the genomic Cell Cycle Progression Score can be utilized as a predictor for grade change.

Methods

Lehigh Valley Hospital is a large, mixed rural/urban teaching hospital. For this IRB-approved retrospective analysis, we evaluated men with PCa who underwent treatment with RP between 2015 and 2017.

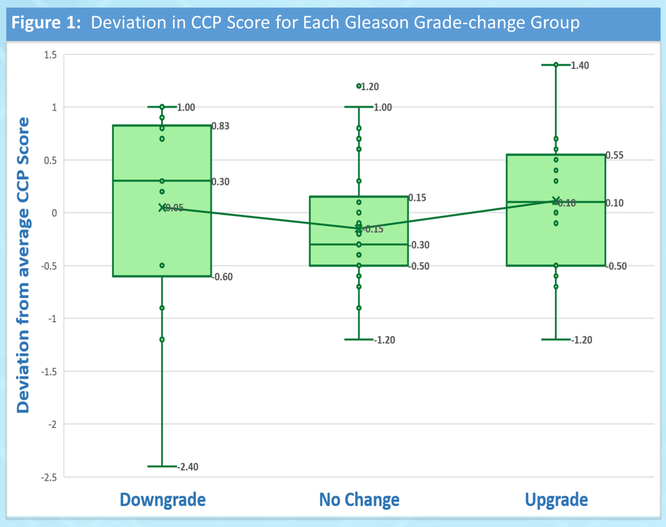
- Patients stratified by AUA risk score: low (LR)-, intermediate (IR)-, and high-risk (HR) groups
- Sub-grouped by change in GS: upgraded, downgraded, or no change, i.e. 3+4 → 4+3 is an upgrade
- CCPS for each patient normalized with 0=average in each respective AUA risk group, using information from Prolaris Score Report (based on data collected by Myriad Genetics)
  - Negative numbers less aggressive, Positive numbers more aggressive
- Mean CCPS deviation for each GS-change subgroup calculated to assess for correlation between grade-change and CCPS-predicted risk.

Less Aggressive **CCPS Deviation** **More Aggressive**

-3 ← 0 → +3

Results

Figure 1: Deviation in CCP Score for Each Gleason Grade-change Group



- 65 Men underwent radical prostatectomy after Prolaris analysis between 2015-2017: **Table 1**
  - 63% with biopsy GS ≤ 3+4
  - 49% rate of GS discordance: 21.5% downgraded, 27.7% upgraded
- Mean CCPS deviation for each group detailed in **Table 2**
- One-way ANOVA showed no significant difference in CCPS between grade-change groups (p = 0.5532)
  - ANOVA of Intermediate-risk group (n=44) also showed no significant difference (p = 0.4196)
- 7 of 22 with CCPS deviation <-0.3 had GS upgrade and 8 of 15 with deviation -0.2 to 0.2 had GS discordance (**Figure 2**)
- Mean CCPS deviation in no-change group was within "consistent" range (-0.18 ± 0.56) but not statistically different from other groups and had significant deviation
- Intermediate-risk group had nearly even distribution of CCPS deviation between GS grade-change subgroups (**Figure 3**)

Patient Demographics (n=65)		
Age at surgery	mean ± sd	62.0 ± 7.2
AUA Risk	Low	12 (18.5%)
	Intermediate	44 (67.7%)
	High	9 (13.8%)
Biopsy Gleason	3+3	10 (15.4%)
	3+4	33 (50.8%)
	4+3	15 (23.1%)
	4+4	6 (9.2%)
	4+5	1 (1.5%)
Cell Cycle Progression Score	1-2.4	4 (6.1%)
	2.5-3.5	35 (53.8%)
	3.6-5	26 (40.0%)
Difference from Average CCP	<-0.8	9 (13.8%)
	-0.8 to -0.3	19 (29.2%)
	-0.2 to 0.2	15 (23.1%)
	0.3 to 0.8	16 (24.6%)
	>0.8	6 (9.2%)
Gleason Grade Changes	Downgrade	14 (21.5%)
	No Change	33 (50.8%)
	Upgrade	18 (27.7%)

Table 1: Patient characteristics. CCP Scores normalized to 0=average risk for each individual AUA risk group

	Downgraded (N=14)	No Change (N=33)	Upgraded (N=18)
Total (N=65)	0.05 ± 0.98	-0.18 ± 0.56	0.04 ± 0.75
AUA High Risk (N=9)	-0.22 ± 1.32 (N=6)	-0.57 ± 0.58 (N=3)	N/A
AUA Int. Risk (N=44)	0.00 ± 0.72 (N=8)	-0.10 ± 0.58 (N=23)	0.21 ± 0.75 (N=13)
AUA Low Risk (N=12)	N/A	-0.31 ± 0.44 (N=7)	-0.40 ± 0.61 (N=5)

Table 2. Average CCPS change for GS grade-change groups

Figure 3: Average CCP Score deviation for GS grade-change groups in intermediate-risk pool

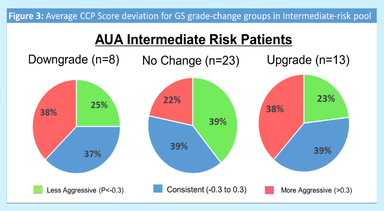


Figure 4: Average CCP Score deviation for GS grade-change groups in entire group

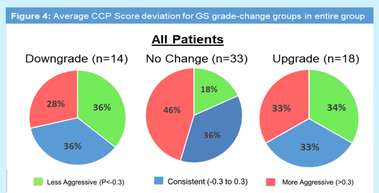
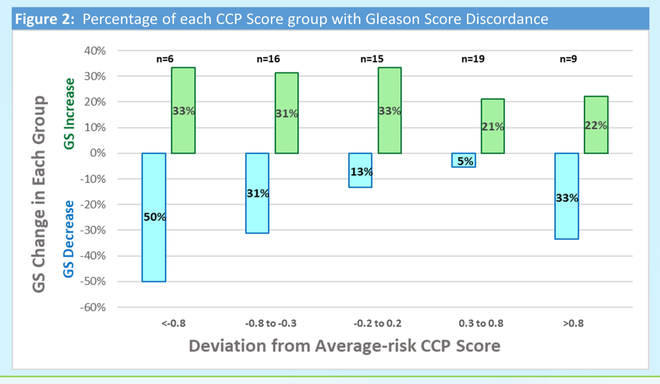


Figure 2: Percentage of each CCP Score group with Gleason Score Discordance



Discussion

- Several management options exist for men with LR and IR PCa
  - Decision to undergo surgery vs. surveillance dependent on degree of risk and patients' wishes
  - High degree of Values-based Patient-centered Care (VBPCC) required in decision-making
  - Genomics shown to alleviate some of mental treatment burden in PCa patients[4]
- Prognostication with GS high degree of variance
  - Literature discordance rate: 30%[1]
  - Study discordance rate: 49%
- Our results do not suggest predictive ability of CCPS to determine final pathologic GS
  - "Consistent" CCPS does not guarantee GS concordance
  - VBPCC conversations able to use GS and CCPS score as independent risk-stratification tools
- Limitations: smaller than expected sample size (many more prostatectomies than genomic tests)
  - Will standardize consent for genomic testing in future protocols

Conclusions

When analyzed as a whole, and when stratified by AUA risk, there was no correlation between average CCPS deviation and grade change from biopsy to post-RP pathology. Furthermore, there was no significant difference between average CCPS scores in the different grade-change groups. Our data suggest that the CCPS may not be used to reliably predict a change in biopsy GS.

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